REMARKS

Claims 1-4, 6-47 and 70-80 are presently pending herein. Claim 5 and withdrawn claims 48-69 having been cancelled above without prejudice or disclaimer.

Claims 73-80 have been added. Support for these new claims can be found, for example, in paragraphs [0057], [0061] and [0062] and in original claim 35. Thus, no new matter is added.

Claims 1, 2, 6, 7, 9, 13, 18-20, 22, 23, 39 and 72 have been amended above.

Most of these claim amendments are self explanatory. For example, claims 18, 19, 20 and 22 have been amended to clarify that it is the matrix polymer *region* (rather than the matrix polymer), which contains the bioactive agents and radio-opacifying agent.

Previously existing elements of claims 1 and 72 have been rearranged to recite the bioactive agents prior to the recitation of the at least one matrix polymer region. (It was found that this organizational structure is less awkward that the reverse structure, in which the one or more matrix polymer regions are claimed prior to the bioactive agents.)

Additional elements have also been added to claims 1 and 72. Support for these additional elements can be found, for example, in paragraphs [0010], [0012], [0027], [0029], [0032], [0034] and [0090] of the specification and in original claims 5 and 35. No new matter is added.

Rejection of Claims under 35 U.S.C. 102(e)--Darouiche

Claims 1-8, 13-19, 26, 27, 31 and 70-72 are presently rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 6,475,434 (Darouiche).

Applicants respectfully traverse this rejection and its supporting remarks.

For example, each of claims 1 and 72, the only independent claims presently pending, is presently directed to an implantable or insertable medical device that comprises: (a) bioactive agents comprising (i) an antimicrobial agent and (ii) a microbial attachment/biofilm synthesis inhibitor selected from NSAIDs, chelating agents, and mixtures thereof; and (b) at least one biocompatible matrix polymer region that comprises (i) one or more polymers and (ii) one or more of the bioactive agents dispersed throughout. At least one of the biocompatible matrix polymer regions within the device is not a medical device coating. Moreover, the bioactive agents are present in the device

in an amount effective to inhibit microbial growth on the device for a period of at least 30 days after implantation or insertion of the device into a subject.

Claims 1 and 72 are patentable over Darouiche for several reasons.

For example, Darouiche is directed to biofilm penetrating agents, in particular, cysteine and derivatives thereof (see, col. 6, lines 18 *et seq.*), whereas the claims 1 and 72 both require a microbial attachment/biofilm synthesis inhibitor selected from NSAIDs (e.g., salicylic acid, its salts or its derivatives), chelating agents, and mixtures thereof. The use of these materials is neither taught nor suggested by Darouiche, and certainly not the use of these materials in combination with an antimicrobial agent as claimed.

Furthermore, Darouiche teaches using the biofilm penetrating agents within a medical device *coating*. See Darouiche Abstract. The devices of claims 1 and 72 on the other hand, contain at least one biocompatible matrix polymer region (which comprises one or more polymers and one or more bioactive agents). At least one matrix polymer region in claims 1 and 72 is *not* a medical device coating. The use of a bioactive-agent-containing biocompatible matrix polymer region, which is not a medical device coating, is neither taught nor suggested by Darouiche.

For at least the above reasons it is respectfully submitted that claims 1 and 72 are neither anticipated by, nor obvious in view of, Darouiche. Claims 2-4, 6-8, 13-19, 26, 27, 31 and 70-71 depend either directly or indirectly from claim 1 and are therefore neither anticipated by nor obvious in view of Darouiche for at least the same reasons as claim 1. Claim 5 has been cancelled.

In view of the above, reconsideration and withdrawal of the rejection of claims 1-3, 7-15, 17, 37, and 40-42 under 35 U.S.C. 102(e) as being anticipated by Darouiche are respectfully requested.

Rejection of Claims under 35 U.S.C. 103(a)—Darouiche, Helmus et al. and Zaffaroni et al.

Claims 9, 10, 11, 12, 26-42, 70 and 71 are presently rejected under 35 U.S.C. 103(a) as being unpatentable over Darouiche and further in view of Helmus et al. (U.S. Patent No. 5,569,463) and Zaffaroni et al. (U.S. Patent No. 4,036,227).

Applicants respectfully traverse this rejection and its supporting remarks.

For example, as noted above each of claims 1 and 72 is patentable over Darouiche. For example, Darouiche neither teaches nor suggests the use of a microbial attachment/biofilm synthesis inhibitor selected from NSAIDs (e.g., salicylic acid, its salts or its derivatives), chelating agents, and mixtures thereof. Nor does Darouiche teach or suggest such a microbial attachment/biofilm synthesis inhibitor in combination with an antimicrobial agent.

Helmus et al., which is cited for its teaching of ethylene vinyl acetate[1], does not make up for the above deficiencies in Darouiche. The same is true for Zaffaroni et al.[2]

For at least the above reasons it is respectfully submitted that independent claims 1 and 72 are patentable over Darouiche in view of Helmus et al. and Zaffaroni et al.

Claims 9, 10, 11, 12, 26-42, 70 and 71 depend either directly or indirectly from claim 1 and are therefore patentable over Darouiche in view of Helmus et al. and Zaffaroni et al. for at least the same reasons as claim 1.

For at least these reasons, reconsideration and withdrawal of the rejection of claims 9, 10, 11, 12, 26-42, 70 and 71 under 35 U.S.C. 103(a) as being unpatentable over Darouiche in view of Helmus et al. and Zaffaroni et al. are respectfully requested.

Rejection of Claims under 35 U.S.C. 103(a)—Darouiche and Braden

Claims 20-22 are presently rejected under 35 U.S.C. 103(a) as being unpatentable over Darouiche and further in view of Braden (U.S. Patent No.5,468,787).

Applicants respectfully traverse this rejection and its supporting remarks.

For example, as noted above, each of claims 1 and 72 is patentable over Darouiche. For example, Darouiche neither teaches nor suggests the use of a microbial attachment/biofilm synthesis inhibitor selected from NSAIDs (e.g., salicylic acid, its salts or its derivatives), chelating agents, and mixtures thereof. Nor does Darouiche teach or

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[1] It is also noted, for example, that Helmus et al. and Zaffaroni et al. do not appear to teach the specific vinyl acetate content of claims 11 and 12.

[2] It is noted that Zaffaroni et al. is directed to osmotic devices, including oral devices, which are comprised of a wall surrounding and forming a compartment (as a means for containing a useful agent)and having a passageway for releasing the agent. See Zaffaroni et al. Abstract. Hence, the delivery mechanism of Zaffaroni et al. differs dramatically from that of bioactive-agent-containing biocompatible matrix polymer regions, such as are claimed herein.

suggest such a microbial attachment/biofilm synthesis inhibitor in combination with an antimicrobial agent.

Braden, which is cited for its disclosure of a base matrix having a radioopacifying agent incorporated therewith, does not make up for the above deficiencies in Darouiche.

For at least the above reasons it is respectfully submitted that claims 1 and 72 are patentable over Darouiche in view of Braden.

Claims 20-22 depend, either directly or indirectly, from claim 1 and are therefore patentable over Darouiche in view of Braden for at least the same reasons as claim 1.

For at least these reasons, reconsideration and withdrawal of the rejection of claims 20-22 under 35 U.S.C. 103(a) as being unpatentable over Darouiche in view of Braden are respectfully requested.

Rejection of Claims under 35 U.S.C. 103(a)—Darouiche and Capelli

Claims 23-25 are presently rejected under 35 U.S.C. 103(a) as being unpatentable over Darouiche and further in view of Capelli (U.S. Patent No. 5,607,683).

Applicants respectfully traverse this rejection and its supporting remarks.

For example, as noted above each of claims 1 and 72 is patentable over Darouiche. For example, Darouiche neither teaches nor suggests the use of a microbial attachment/biofilm synthesis inhibitor selected from NSAIDs (e.g., salicylic acid, its salts or its derivatives), chelating agents, and mixtures thereof. Nor does Darouiche teach or suggest the combination of such a microbial attachment/biofilm synthesis inhibitor with an antimicrobial agent.

Capelli, which is cited for is disclosure of various therapeutic agents[3], does not make up for the above deficiencies in Darouiche.

For at least the above reasons it is respectfully submitted that claims 1 and 72 are patentable over Darouiche in view of Capelli.

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[3] Capelli was apparently cited for its teaching of various therapeutic agents, including cisplatin. It is noted, however, that cisplatin is apparently only mentioned in the background of the invention. Furthermore, it is noted that Capelli is directed to "compositions [that] are useful for topical treatment of infections caused by bacteria, fungus and viruses in humans and animals and for *treating* medical devices, foams and adhesives to impart infection-resistance." See Capelli Abstract (emphasis added). Hence, Capelli is drawn to treating preexisting device structures.

Claims 23-25 depend, either directly or indirectly, from claim 1 and are therefore patentable over Darouiche in view of Capelli for at least the same reasons as claim 1.

For at least these reasons, reconsideration and withdrawal of the rejection of claims 23-25 under 35 U.S.C. 103(a) as being unpatentable over Darouiche in view of Capelli are respectfully requested.

Rejection of Claims under 35 U.S.C. 103(a)—Darouiche and Redkar et al.

Claims 43-47 are presently rejected under 35 U.S.C. 103(a) as being unpatentable over Darouiche and further in view of Redkar et al. (U.S. Patent No.6,482,830).

Applicants respectfully traverse this rejection and its supporting remarks.

For example, Redkar et al., which is directed to compositions and formulations containing 9-nitrocamptothecin polymorphs, is cited for its disclosure of "the use of a catheter or a stent for treatment of the pancreas wherein the device comprises a bicarbonate buffering agent." However, it is not seen where such a teaching is found in Redkar et al. The examiner is requested to point out the specific teachings in Redkar et al. upon which he is relying for support of this proposition, so that a proper response can be considered.

Moreover, as noted above each of claims 1 and 72 is patentable over Darouiche. For example, Darouiche neither teaches nor suggests the use of a microbial attachment/biofilm synthesis inhibitor selected from NSAIDs (e.g., salicylic acid, its salts or its derivatives), chelating agents, and mixtures thereof. Nor does Darouiche teach or suggest such a microbial attachment/biofilm synthesis inhibitor in combination with an antimicrobial agent.

Regardless of the teachings of Redkar et al. vis-à-vis buffering agents, Redkar et al. does not make up for these deficiencies in Darouiche.

For at least the above reasons, it is respectfully submitted that claims 1 and 72 are patentable over Darouiche in view of Redkar.

Claims 43-47 depend, either directly or indirectly, from claim 1 and are therefore patentable over Darouiche in view of Redkar for at least the same reasons as claim 1.

For at least these reasons, reconsideration and withdrawal of the rejection of claims 43-47 under 35 U.S.C. 103(a) as being unpatentable over Darouiche in view of Redkar are respectfully requested.

Rejection of Claim 72 under 35 U.S.C. 103(a)—Darouiche, Helmus et al., Zaffaroni et al. and Braden et al.

Claim 72 is presently rejected under 35 U.S.C. 103(a) as being unpatentable over Darouiche in view of Helmus et al., Zaffaroni et al. and Braden.

Applicants respectfully traverse this rejection and its supporting remarks.

For example, as noted above, each of claims 1 and 72 is patentable over Darouiche. For example, Darouiche neither teaches nor suggests the use of a microbial attachment/biofilm synthesis inhibitor selected from NSAIDs (e.g., salicylic acid, its salts or its derivatives), chelating agents, and mixtures thereof. Nor does Darouiche teach or suggest such a microbial attachment/biofilm synthesis inhibitor in combination with an antimicrobial agent.

As also noted above, Helmus et al., Zaffaroni et al. and Braden do not make up for the above deficiencies in Darouiche.

For at least the above reasons it is respectfully submitted that claims 1 and 72 are patentable over Darouiche in view of Helmus et al., Zaffaroni et al. and Braden.

Reconsideration and withdrawal of the rejection of claim 72 under 35 U.S.C. 103(a) as being unpatentable over Darouiche in view of Helmus et al., Zaffaroni et al. and Braden are respectfully requested.

CONCLUSION

Applicants submit that the claims of the present invention are in condition for allowance, early notification of which is earnestly solicited.

FEES

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